Notice of Allowability	Application No.	Applicant(s)	
	10/797,487	GOODFELLOW ET AL.	
	Examiner	Art Unit	
	Anthony J. Paviglianiti	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *election of invention by telephone on March 31, 2005*.

2. ☒ The allowed claim(s) is/are *1 - 57, 59 and 60*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date 11/8/04
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

Claims 1 – 63 were pending in the application. In response to the examiner's restriction requirement, below, Applicant elected the invention of **Group I (Claims 1 – 57)** by telephone; accordingly, **Claims 58 – 63** were withdrawn from further consideration as being drawn to a non-elected invention pursuant to 37 C.F.R. §1.142(b). However, after examination of the elected invention, the claimed chemical compounds of the invention were determined to be free of the prior art and allowable, so the requirement for restriction was expressly withdrawn by the examiner and **Claims 58 – 63** were rejoined for examination. **Claims 58, 61, 62, and 63** were subsequently cancelled by Examiner's Amendment with authorization by the applicant. Therefore, **Claims 1 – 57** and **Claims 59 – 60** are currently pending in the application and were examined on the merits for patentability. An Examiner's Amendment follows the analysis below.

Priority

The present application claims priority to U.S. Provisional Application No. 60/452,709, filed March 7, 2003.

Information Disclosure Statement

The Information Disclosure Statement filed on November 8, 2004, is in compliance with 37 C.F.R. §1.97, and was considered by the examiner.

Election/Restrictions and Rejoinder of Claims

Applicant's election, with traverse, of the invention of **Group I (Claims 1 – 57)**, by telephone on March 31, 2005, is respectfully acknowledged, as well as the individual compound of formula (I) represented by Example 11-39 (Specification at page 47). However, after extensive examination of the prior art concerning the elected invention of **Claims 1 – 57**, the

examiner determined that the claimed compounds were free of the prior art and were directed to an allowable product. Pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86), claims which were directed to the process of making or using the patentable product, previously withdrawn from consideration as a result of a restriction requirement, are now subject to being rejoined. **Claims 58 – 63 are hereby rejoined to be examined for patentability under 37 C.F.R. §1.104.**

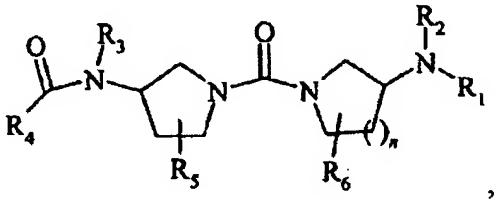
Since all claims previously withdrawn from consideration under 37 C.F.R. §1.142 have been rejoined, the restriction requirement made by telephone (and shown below), is hereby expressly withdrawn by the examiner.

Applicant's traversal of the restriction, on grounds that, "the compound and composition claims and 'method of use' claims in this case are within the same invention and entitled to be examined together consonant with in re Ochiai," is made moot by the rejoinder of method of use claims for examination, and will therefore not be addressed.

The restriction requirement (prior to rejoinder) had been as follows:

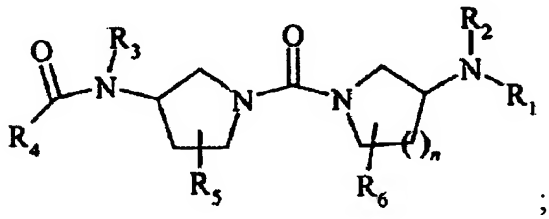
The Markush groups set forth in the claims include both independent and distinct inventions, and patentably distinct compounds (or species) within each invention. However, this application discloses and claims a plurality of patentably distinct inventions far too numerous to list individually. Moreover, each of these inventions contains a plurality of patentably distinct compounds, also far too numerous to list individually. **For these reasons provided below, restriction to one of the following inventions is required under 35 U.S.C. 121,** wherein an Invention is a set of patentably distinct inventions of a broad statutory category (e.g., compounds, methods of use, methods of making, etc.):

I. **Claims 1 - 57**, drawn to compounds of formula



, depicted in **Claim 1**, classified in Class 548, subclass 524, and 953; and other subclasses.

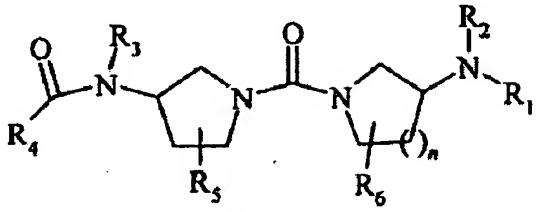
II. **Claims 57 – 63**, drawn to methods of using compounds of formula



; classified in Class 514, subclass 210.18, 422, and other subclasses.

In addition to an election of one of the above Groups, restriction is further required under 35 U.S.C. §121 as follows:

In accordance with the decisions in In re Harnisch, 631 F.2d 716, 206 USPQ 300 (CCPA 1980) and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App & Int. 1984), restriction of a Markush group is proper where the compounds with the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. §103 with respect to the other member(s).

Therefore, when one of **Groups I - II** is elected, **an election of a single compound of general formula**  **is further required**, including an exact definition of each substitution on the base molecule, wherein a single member at each substituent group is selected. For example, if the base molecule of the formula has substituent groups (in order of appearance) R_4, R_3, R_5, R_6, **n**, R_2, R_1, R_7, R_8, and R_9, then applicant must select a single substituent representing R_4, such as "R_4 is 2-[5-(4-ethylphenyl)thienyl]," as well as specific values at each subsequent variable position (R_3, R_5, R_6, **n**, R_2, R_1, R_7, R_8, and R_9), so that a single identifiable compound is selected.

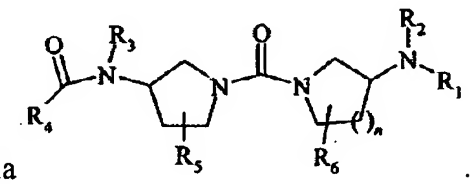
One suggestion for the election of a compound would be to select one of the examples of the invention disclosed in the Specification, such as one of the embodiments in the Table following Example 12 (p. 48, line 3), including Examples 12-1 through 12-52 (page 48, line 16 through page 51, line 1).

Further, if **Group II** is elected, then **election of a specific method of use, *along with an elected compound of general formula (II)*, is required**; for example, a method of treating:

A. obesity;

B. anxiety or depression;

C. digestive disorder; etc.

using an "elected" compound of the general formula 

In the instant case, upon election of a single compound, the Office will review the claims and disclosure to determine the scope of the independent invention encompassing the elected compound (compounds which are so similar as to be within the same inventive concept and reduction to practice). The scope of an independent invention will encompass all compounds within the scope of the claim which fall into the same class and subclass as the elected compound, but may also include additional compounds which fall in related subclasses.

Examination will then proceed on the elected compound *and* the entire scope of the invention encompassing the elected compound as defined by common classification. A clear statement of the examined invention, defined by those class(es) and subclass(es) will be set forth in the first action on the merits.

Note that the restriction requirement will not be made final until such time as Applicant is informed of the full scope of compounds along with (if appropriate) the process of using or making the compounds under investigation. This will be set forth by reference to specific class(es) and subclass(es) examined.

Should Applicant traverse on the ground that the compounds are not patentably distinct, Applicant should submit evidence or identify such evidence now of record showing the compounds to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. §103(a) of the other invention.

All compounds falling outside of the class(es) and subclass(es) of the selected compound and any other subclass encompassed by the election above will be directed to non-elected subject matter and will be withdrawn from consideration under 35 U.S.C. §121 and 37 C.F.R. §1.142(b).

Applicant may reserve the right to file divisional applications on the remaining subject matter. The provisions of 35 U.S.C. §121 apply with regard to double patenting covering divisional applications.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. §1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 C.F.R. §1.48(b) and by the fee required under 37 C.F.R. §1.17(i).

If desired upon election of a single compound, applicants can review the claims and disclosure to determine the scope of the invention and can set forth a group of compounds which are so similar within the same inventive concept and reduction to practice. Markush claims must be provided with support in the disclosure for each member of the Markush group. See MPEP §608.01(p). Applicant should exercise caution in making a selection of a single member for each substituent group on the base molecule to be consistent with the written description.

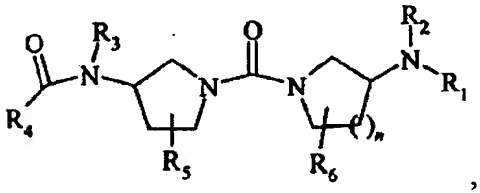
Rationale Establishing Patentable Distinctiveness Within Each Group

Each Group listed above is directed to or involves the use of compounds which are recognized in the art as being distinct from one another because of their diverse chemical structure, their different chemical properties, modes of action, different effects and reactive conditions (MPEP §806.04, MPEP §808.01). Additionally, the level of skill in the art is not such that one invention would be obvious over the other invention (Group); i.e., they are patentable over each other. Chemical structures which are similar are presumed to function similarly, whereas chemical structures that are not similar are not presumed to function similarly. The

presumption even for similar chemical structures though is not irrebuttable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holding of Application of Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984), chemical structures are patentably distinct where the structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure.

The above Groups represent general areas wherein the inventions are independent and distinct, each from the other, because of the following reasons:

Group I and **Group II** are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). The process for using the compounds of formula



, such as for treatment of anxiety or depression (as in **Claim 60**), can be practiced with another materially different product, such as amitriptyline. See, e.g., Whooley, M., and Simon, G., "Managing Depression in Medical Outpatients," New Engl. J. Med., vol. 343(26), pages 1942 – 1950 (Dec. 2000), at p. 1946, line 4 (Table 4). **Group I** and **Group II** are therefore separate and distinct inventions for which restriction is appropriate.

In addition, because of the multiple classes and subclasses across each of the Groups, and the divergent searches of the prior art that would be required for examination of all the inventions, a serious burden is imposed upon the examiner to perform a complete search of the defined areas. Therefore, for the reasons given above, the restriction set forth is proper, and not to restrict would impose a serious burden in the examination of this application.

Advisory of Rejoinder

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

During a telephone call with Karl R. Hermanns, Esq. on March 31, 2005, the above restriction requirements were discussed, and applicant elected Group I, with traverse, and the compound of formula (I) represented by Example 11-39 (Specification at page 47). The election with traverse was made on the grounds that "the compound and composition

claims and 'method of use' claims in this case are within the same invention and entitled to be examined together consonant with In re Ochiai" [cited above].

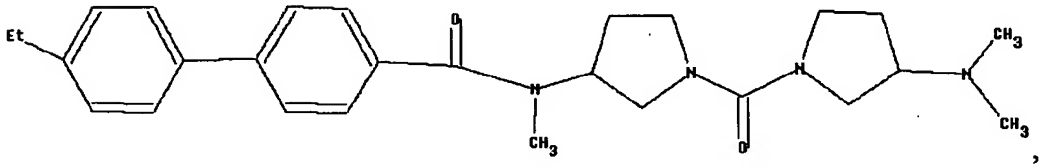
Applicant is advised that the reply to this requirement to be complete must include an election of the Invention to be examined even though the requirement be traversed. 37 C.F.R. §1.143.

Applicant is further advised that a reply to this requirement must identify the specific compound that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Scope of Prior Art Searched

1) The elected compound

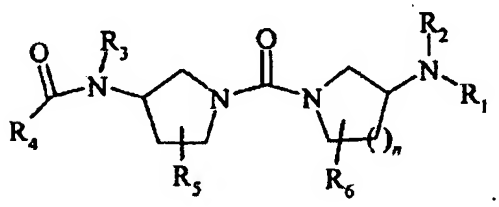
The chemical compound elected by applicant,



, was searched in the applicable art, and is free of the prior art of record.

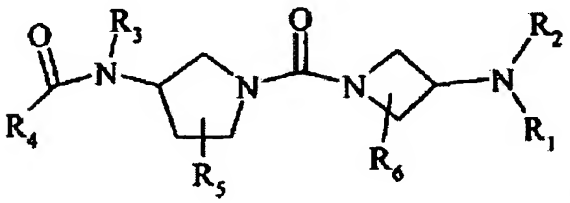
2) Expansion of search of prior art

The search of the art was expanded beyond the elected compound by a series of expanding searches corresponding to the compounds of formula (I)

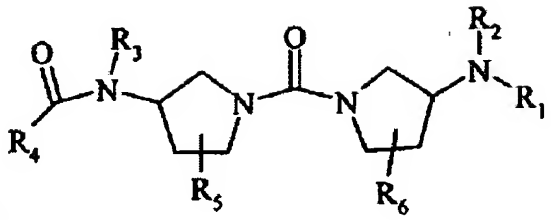


. The expanding searches ultimately covered all chemical

derivatives having the following two major core structures:



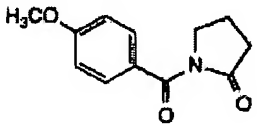
and



(i.e., formula (I) wherein ***n*** is 0 and 1, respectively), and each was found to be free of the prior art, even with the broadest limitations for substituents $\mathbf{R_1}$, $\mathbf{R_2}$, $\mathbf{R_3}$, $\mathbf{R_4}$, $\mathbf{R_5}$ and $\mathbf{R_6}$ in **Claims 1 – 57**.

*3) **Method of use claims (after rejoinder)***

The Specification discloses data and journal references supporting a method of treating obesity, anxiety and depression, by administering a compound or composition of formula (I). See Specification at page 1, lines 12 – 29 (journal references on melanin-concentrating hormone (MCH) and obesity); page 12, lines 20 – 22 (*in vitro* data for examples of present invention and binding to MCH receptors), page 13, lines 8 – 17; page 14, lines 19 – 33 and page 15, lines 1 – 10 (animal study models for obesity); page 15, lines 11 – 25 (animal study models for anxiety). In addition, the prior art at the time of this application disclosed other "pyrrolidinyl-carbonyl" compounds for treatment of anxiety and depression, such as "aniracetam"



(see, e.g., U.S. Patent No. 5,652,249, at col. 1, lines 23 – 26, "...aniracetam which is a recently launched nootropic drug is expected to have ameliorative effects on emotional disturbances (anxiety, impatience, depressed mood) after brain infarct"); see also Nakamura, K. and Tanaka, Y., "Antidepressant-like effects of aniracetam in aged rats and its mode of action," Psychopharmacology, vol. 158(2), pages 205 – 212 (Nov. 2001), at Abstract; p. 210, col. 2, lines

58 – 59 and p. 211, lines 1 – 2 ("in conclusion, aniracetam effectively improved the forced swim stress-induced immobility in aged rats with hypo-dopaminergic and –serotonergic activiy, but not in young rats.").

Therefore, the data and journal references disclosed in the Specification or known in the art were determined to be sufficiently enabling to one of skill in the art to make and use the present invention with the limitations of **Claims 59** and **60.**

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R. §1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Agreement for the following examiner's amendment as to **Claims 58, 61, 62** and **63** was reached in a telephone interview with Karl R. Hermanns, Esq., on June 15, 2005, and authorized by Mr. Hermanns. The agreement and authorization are also summarized on the Telephone Interview Summary Form (PTOL-413) dated June 15, 2005. Agreement to the examiner's amendment to correct minor typographical errors in **Claims 26, 28, 37, 44 and 46** was reached in a telephone call to Mr. Hermanns on June 20, 2005.

The claims in the application have been amended as follows:

In **Claim 26**, page 81, line 32, delete "tetrohydropyranyl" and insert ---tetrahydropyranyl---.

In **Claim 28**, page 82, line 4, delete "tetrohydropyranylmethyl" and insert ---tetrahydropyranylmethyl---.

In **Claim 28**, page 82, line 5, delete "tetrohydropyranyl" and insert ---tetrahydropyranyl---.

In **Claim 37**, page 83, line 3, delete "methyl phenyl" and insert ---methylphenyl---.

In **Claim 44**, page 83, line 24, delete "tetrohydropyranyl" and insert ---tetrahydropyranyl---.

In **Claim 46**, page 83, line 30, delete "tetrohydropyranylmethyl" and insert ---tetrahydropyranylmethyl---.

In **Claim 46**, page 83, line 31, delete "tetrohydropyranyl" and insert ---tetrahydropyranyl---.

Delete **Claim 58**, page 84, lines 31 – 33.

Delete **Claim 61**, page 85, lines 9 – 11.

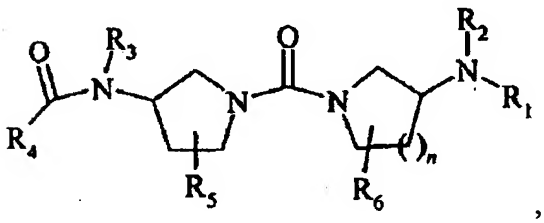
Delete **Claim 62**, page 85, lines 13 - 15.

Delete **Claim 63**, page 85, lines 17 - 19.

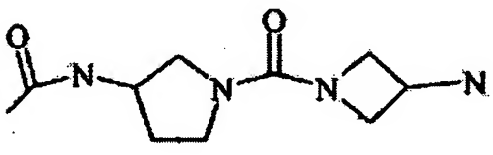
The deleted claims were canceled by applicant without prejudice to pursue in a future continuing or divisional application.

Reasons for Allowance

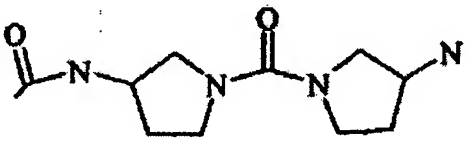
The present invention is directed to compounds and compositions of formula (I)



, wherein ***n*** is 0 or 1, such that the chemical structures encompassed by the invention include those with the core structures:



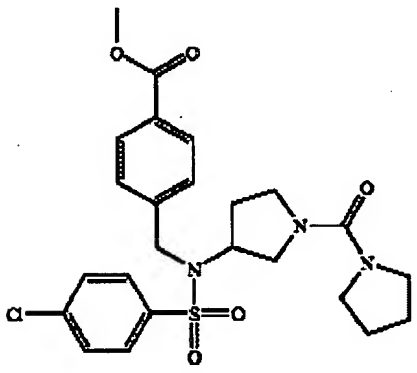
and



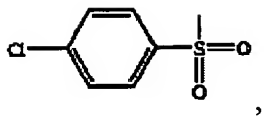
, respectively, as well as methods of treating obesity, anxiety and/or depression by administering a compound or composition of formula (I).

Specifically, the compounds of the present invention were free of the prior art because all of the claimed compounds shared the limitations of two fully-saturated pyrrolidinyl rings (or a pyrrolidinyl and an azetidinyl ring) *directly linked to the same carbonyl group through the nitrogen atom*, where one pyrrolidinyl ring was substituted by an "amino-carbonyl" group at its 3-position on the ring, and the other pyrrolidinyl (or azetidinyl) ring was substituted by an "amino" group at the 3-position on the ring, as shown in formula (I) above. When the above limitations were imposed, even the broadest interpretation of the limitations of substituent groups **R_1, R_2, R_3, R_4, R_5** and **R_6** in **Claims 1 – 57** were not anticipated nor rendered obvious by known chemical compounds in the prior art.

The closest prior art was the compound disclosed in **WO 03/013527 A1** (publication date Feb. 20, 2003), to Hubert Josien, et al., who disclosed the compound



(see WO 03/013527 A1 at page 45, line 4, "Example 114"). The prior art contains two fully-saturated pyrrolidinyl rings bound through their nitrogen atoms to the same carbonyl group, and one of the pyrrolidinyl rings has an "amino" group at the 3-position on the ring. However, the prior art differs from the compounds of the present invention because it lacks altogether the requisite "amino carbonyl" substituent on the second pyrrolidinyl

ring. Another difference is that the prior has a substituent at the $\mathbf{R_2}$ position,  , which is outside of the limitations of the present invention. The present invention requires $\mathbf{R_2}$ to be, *inter alia*, $-S(O)_2R_8$, where $\mathbf{R_8}$ is limited to "*hydrogen, alkyl, substituted alkyl*," and would not include "4-chlorophenyl," as found in the prior art.

Therefore, based on the analysis above, **Claims 1 – 57** and **Claims 59 – 60**, as amended by the Examiner's Amendment authorized by applicant, are neither anticipated nor rendered obvious over the prior art of record, and are allowable.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

After examination of the chemical compounds of the elected invention, the restriction requirement described above was expressly withdrawn by the examiner, and **Claims 58 – 63** were rejoined for examination on the merits.

Claims 58, 61, 62 and **63** were canceled by applicant, as in the Examiner's Amendment authorized by applicant (above).

Claims 1 – 57 and **Claims 59 – 60**, as amended by the Examiner's Amendment authorized by applicant (above), are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Anthony J. Paviglianiti** whose telephone number is **(571) 272-3107**. The examiner can normally be reached on Monday-Friday, 8:30 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane, can be reached at (571) 272-0699. **The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300. Please note that this is a new central FAX number for all official correspondence.**

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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